

homozygotes, GC heterozygotes and CC homozygotes (16, 0-256; 32, 0-256; 32, 0-64, respectively; $p=ns$). Conclusion: Our data suggest that the C (-260) T polymorphism in the promoter region of the CD14 receptor gene and the G (-174) C polymorphism of the Interleukin 6 gene, are not involved in modulation of the individual immune response to Cp infection in patients with ischaemic heart disease.

1136-89

Beta-2 Receptors Are Upregulated in Canine Ventricles With a Chronic Myocardial Infarction

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Background: Beta-1-adrenergic receptor densities decrease in end-stage cardiomyopathy with no significant change in beta-2 or alpha receptor density. The relative densities of beta-receptors after myocardial infarction (MI) with normal left ventricular function are less well understood. This study examined beta-receptor densities in normal dogs and compared them with animals 45 days after MI.

Methods: Four dogs were instrumented with an anterior MI by permanent ligation of the left anterior descending (LAD) coronary artery during lateral thoracotomy. 45 days were allowed for recovery and ventricular tissue was harvested during a terminal experiment. Tissue in the LAD distribution was compared with tissue in the circumflex (Cx) territory in post-MI dogs and normal animals ($n=15$). beta-receptor densities were measured with receptor specific quantitative film autoradiography.

Results: beta-receptors from normal animals were not different between the LAD (7.6 ± 3 fmol/mg, 76% beta-1; 2.3 ± 0.6 fmol/mg, 23%, beta-2) and Cx (7.1 ± 0.8 fmol/mg, 75% beta-1; 2.3 ± 0.2 fmol/mg, 25%, beta-2) tissues. Beta-2 receptor densities in post-MI dogs were higher ($p<0.04$) in both the LAD (7.4 ± 2 fmol/mg, 63%, beta-1; 4.3 ± 1 fmol/mg, 37%, beta-2) and the Cx (5.6 ± 2 fmol/mg, 54%, beta-1; 4.7 ± 2 fmol/mg, 46%, beta-2) territories, while beta-1 receptor densities did not change.

Conclusions: Beta-2 adrenergic receptor densities increase following chronic MI and comprise a larger percentage of available adrenergic receptors in canine ventricles. These data may help explain why nonselective beta-blockers tend to be more effective in post-MI clinical populations

1136-90

Relation of the -174 G/C and -572 G/C Promoter Polymorphisms of the Interleukin-6 Gene to Interleukin-6 and Highly Sensitive C-Reactive Protein Serum Levels and to the Extent of Infarction in Acute Myocardial Infarction

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Background: GG homozygotes for -174 G/C polymorphism and carriers of C allele for 572 G/C have higher interleukin-6 (IL-6) levels and longer hospital stays after surgical coronary revascularization. Our aim was to test the hypothesis that promoter polymorphisms of the IL-6 gene may be associated with the extent of acute myocardial infarction (AMI), and the degree of immunological response in AMI.

Methods: We enrolled 50 patients with the diagnosis of AMI. Patients with inflammatory or infectious conditions, malignancy, recent trauma or surgery were excluded. Serum IL-6 and C-Reactive Protein (CRP) levels were determined on admission, and at 48 and 72 hours. Deoxy-ribo nucleic acid was extracted from peripheral blood and amplified with polymerase chain reaction. The -174 G/C and -572 G/C genotypes were determined by using primers. Left ventricular ejection fraction and wall motion score index (WMSI) were calculated on trans-thoracic echocardiography.

Results: There are no significant differences between the GG, GC, and CC groups of both polymorphisms according to infarct localization, therapy, and basal characteristics. Baseline CRP and IL-6 levels were not significantly different, but the 48- and 72-hour CRP and IL-6 levels were significantly higher in -174 GG patients when compared to -174 GC and CC patients.

Ejection fraction was significantly lower and WMSI was significantly higher in -174 GG patients when compared to -174 GC and CC patients.

There were no statistically significant differences between -572 GG and GC (there were no CC) patients according to serum IL-6 and CRP levels, ejection fraction, and WMSI.

Conclusion:

We have demonstrated that GG homozygosity for the -174 G/C polymorphism is associated with higher serum IL-6 and CRP levels, and more extensive infarction evidenced by lower ejection fraction and higher WMSI in AMI. There was no association of the 572 G/C polymorphism with these conditions.

All these associations were independent from factors such as age, gender, diabetes, hypertension, cigarette smoking, prior use of aspirin or statins, infarct localization, therapy, and catheter-based mechanical revascularization.

1136-91

Contribution of Genetic Characteristics of Vascular Adrenergic Receptor to Variant Angina

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Background: The α_2 or β_2 -adrenergic receptor in vasculature mediate vasoconstriction or dilation respectively in response to adrenergic agents, and β_1 -adrenergic receptor in heart mediates chronotropic and inotropic changes. We hypothesized that adrenergic receptor gene polymorphism is associated with vasospastic angina, and would explain the different prevalence of variant angina between Koreans and Caucasians. We investigate the relationship of vasospastic angina and four kinds of adrenergic receptor poly-

morphisms (α_{2c} Del322-325, β_2 Gly16, β_2 Glu27 and β_1 Arg389)

Methods: Vasospastic angina ($N=162$) was confirmed by focal coronary spasm in CAG with chest pain or ST elevation on ECG after ergonovine intravenous infusion. Normal control group comprised 129 subjects who showed normal coronary angiogram. After a diagnostic coronary angiography was performed, four kinds of genotypes were identified separately using different PCR and RFLP methods from the DNA extracted from the peripheral monocytes.

Results: The allele frequencies of four kinds of adrenergic receptor polymorphisms (α_{2c} Del322-325, β_2 Gly16, β_2 Glu27 and β_1 Arg389) in normal control were 0.23, 0.69, 0.53 and 0.17 respectively, and these are different from those of Caucasians (0.04, 0.61, 0.43, 0.73). The differences were prominent in α_{2c} Del322-325 and β_1 Arg389. The frequencies of homozygosity for α_{2c} Del322-325 polymorphism were significantly higher in variant angina group than in control, 16.4% and 0.8% respectively ($p<0.0001$). The homozygosity for β_2 polymorphism of codon 27(Glu27) is much less frequent in variant angina group than in control (29.3% : 49.3%, $p<0.0001$). However, there was no difference in the prevalence of β_2 polymorphism of codon 16(Gly16) or β_1 polymorphism between the two groups.

Conclusion: The Del (322-325) mutant of α_2 -receptor is a new genetic risk factors for variant angina, and the Glu27 allele of the β_2 -adrenergic receptor is a negative risk factor for variant angina. This is the first report in the world to demonstrate the contribution of genetic characteristics of the vascular adrenergic system to coronary vasospasm.

POSTER SESSION

1137

Unstable Ischemic Syndromes: Risk Assessment and Outcomes II

Tuesday, March 09, 2004, Noon-2:00 p.m.

Morial Convention Center, Hall G

Presentation Hour: 1:00 p.m.-2:00 p.m.

1137-77

Long-Term Cost-Effectiveness of Clopidogrel in Patients Having Percutaneous Coronary Intervention Early After Acute Coronary Syndrome: Results From PCI-CURE

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Background: The efficacy of clopidogrel up to 1 year after percutaneous coronary intervention (PCI) following non-ST-elevation acute coronary syndrome (ACS) was demonstrated in PCI-CURE.

Methods: We evaluated long-term cost effectiveness of clopidogrel after PCI during the initial hospitalization in PCI-CURE; patients received clopidogrel pre-treatment ($n=821$) or placebo ($n=909$). After PCI, >80% received open-label ADP-receptor antagonist for ~4 weeks, then study drug for up to 1 year. This PCI-CURE subgroup characterizes US PCI practice pattern. The composite CV death, stroke or MI occurred in 76 (9.3%) clopidogrel vs 116 (12.8%) placebo patients (RR 0.73, $p=0.02$). Hospitalizations were assigned a DRG; costs were estimated from: 1) Medicare, 2) MEDSTAT (private insurance), 3) MEDSTAT age <65 and Medicare age ≥ 65 . Clopidogrel was assigned a cost of \$3.22/day. Lost life expectancy associated with CV death, MI and stroke was estimated from Framingham data, discounted 3%. 95% CIs for costs differences were obtained by bootstrap.

Results:

	Clopidogrel	Placebo	Difference	95% CI
Medicare Cost	\$14,856	\$14,765	\$91	-\$713, \$839
MEDSTAT Cost	\$20,195	\$20,377	-\$182	-\$1,258, \$837
MEDSTAT/Medicare	\$17,832	\$17,987	-\$155	-\$1,131, \$816
Lost Life Expectancy in Years (Framingham)	0.3426	0.4452	0.1027	-0.0452, 0.2581

The incremental cost-effectiveness ratio was \$882/life year gained (LY) with Medicare (37.6% dominant, 4.8% dominated, 90.8% <\$50,000/LY), dominant with MEDSTAT (58.1% dominant, 3.3% dominated, 91.7% <\$50,000/LY), dominant with MEDSTAT/Medicare (56.0% dominant, 3.6% dominated, 92.0% <\$50,000/LY).

Conclusions: Long-term clopidogrel therapy, up to 1 year after early PCI in the setting of ACS, is both effective and highly cost-effective in cost per LY gained.

1137-93

Carvedilol Preserves Cellular Integrity and Improves Outcome in Patients With Chronic Hibernating Myocardium After Revascularization

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Chronic hibernating myocardium (HM) might undergo progressive cellular degeneration and replacement fibrosis due to apoptosis and necrosis in the setting of recurrent myocardial ischemia. Carvedilol has been shown to provide anti-oxidant and anti-apoptotic effects in experimental animal studies in addition to its alpha- and beta-blocking effects.